

*N(R1)(R2)C(R3)C(R4)N(R5)c1nc(R6)c(R7)c(R8)n1

1. (Currently Amended) A compound of structure (I):

A₁ is optionally substituted aryl or heteroaryl:

A₁ and A₂ are is optionally substituted aryl, aryloxy, arylamino or heteroaryl;

R₁, R₂, R₃ and R₄ are independently selected from the group consisting of hydrogen, hydroxyl, and optionally substituted loweralkyl, cycloloweralkyl, alkylaminoalkyl, loweralkoxy, amino, alkylamino, alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, heteroarylcarbonyl, heteroaralkylcarbonyl, aryl and heteroaryl;

R'₁, R'₂, R'₃ and R'₄ are independently selected from the group consisting of hydrogen, and optionally substituted loweralkyl;

R₅, R₆ and R₇ and are independently selected from the group consisting of hydrogen, hydroxy, halo, carboxyl, nitro, amino, amido, amidino, imido, cyano, and substituted or unsubstituted loweralkyl, loweralkoxy, alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, heteroarylcarbonyl, heteraralkylcarbonyl, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkylaminocarbonyloxy, arylaminocarbonyloxy, formyl, loweralkylcarbonyl, loweralkoxycarbonyl, aminocarbonyl, aminoaryl, alkylsulfonyl, sulfonamido, aminoalkoxy, alkylamino, arylamino, aralkylamino, heteroarylamino, heteroaralkylamino, alkylcarbonylamino, alkylaminocarbonylamino, arylaminocarbonylamino, aralkylcarbonylamino, heteroaralkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, amidino, cycloalkyl, cycloamido, cyclothioamido, cycloamidino,

D2 heterocycloamidino, cycloimido, heterocycloimido, guanidiny, aryl, biaryl, heteroaryl, heterobiaryl, heterocyclo, heterocycloalkyl, arylsulfonyl and arylsulfonamido;

and the pharmaceutically salts thereof.

2. - 5. (Canceled)

6. (Original) A compound of claim 1, wherein at least one of A₁ and A₂ is an aromatic ring having from 3 to 10 carbon ring atoms and optionally 1 or more ring heteroatoms.

D3 7. (Currently Amended) A compound of claim 1, wherein ~~at least one of A₁ and A₂~~ is optionally substituted carbocyclic aryl, arylamino or aryloxy.

8. (Original) A compound of claim 6, wherein at least one of A₁ and A₂ is optionally substituted heteroaryl.

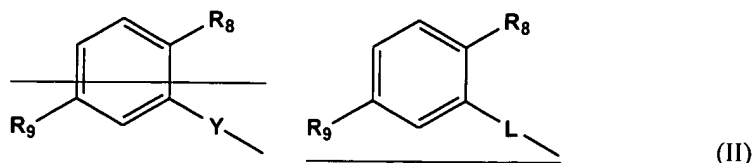
D4 9. (Currently Amended) A compound of claim 1, wherein ~~at least one of A₁ and A₂~~ is selected from the group consisting of substituted or unsubstituted phenylamino and phenyloxy.

10. (Original) A compound of claim 6, wherein at least one of A₁ and A₂ is selected from the group consisting of substituted or unsubstituted pyridyl, pyrimidinyl, thiazolyl, indolyl, imidazolyl, oxadiazolyl, tetrazolyl, pyrazinyl, triazolyl, thiophenyl, furanyl, quinoliny, purinyl, naphthyl, benzothiazolyl, benzopyridly, and benzimidazolyl.

11. (Original) A compound of claim 6, wherein at least one of A₁ and A₂ is substituted with at least one and not more than 3 substitution groups.

12. (Original) A compound of claim 11, wherein said substitution groups are independently selected from the group consisting of nitro, amino, cyano, halo, thioamido, amidino, oxamidino, alkoxyamidino, imidino, guanidino, sulfonamido, carboxyl, formyl, loweralkyl, haloloweralkyl, loweralkoxy, haloloweralkoxy, loweralkoxyalkyl, loweralkylaminoloweralkoxy, loweralkylcarbonyl, loweraralkylcarbonyl, lowerheteroaralkylcarbonyl, alkylthio, aminoalkyl and cyanoalkyl.

13. (Currently Amended) A compound of claim 1, wherein ~~at least one of A₁ and A₂~~ has the formula:



wherein Y L is $-\text{NH}_2$ or $-\text{O}-$; and

R_8 and R_9 are independently selected from the group consisting of hydrogen, nitro, amino, cyano, halo, thioamido, amidino, oxamidino, alkoxyamidino, imidino, guanidiny, sulfonamido, carboxyl, formyl, loweralkyl, haloloweralkyl, loweralkoxy, haloloweralkoxy, loweralkoxyalkyl, loweralkylaminoloweralkoxy, loweralkylcarbonyl, loweraralkylcarbonyl, lowerheteroaralkylcarbonyl, alkylthio, aryl and aralkyl.

14. (Previously Amended) A compound of claim 13, wherein R_8 and R_9 are selected from the group consisting of halo and haloloweralkyl.

15. (Previously Amended) A compound of claim 14, wherein R_8 and R_9 are halo.

D6 16. (Currently Amended) A compound of claim 13, wherein at least one of A1 and A2 is selected from the group consisting of 2,5-dichlorophenylamino and 2,5-dichlorophenyloxy.

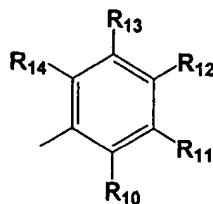
17. (Original) A compound of claim 1, wherein at least one of R₁, R₂, R₃ and R₄ is substituted loweralkyl selected from the group consisting of hydrogen, unsubstituted or substituted loweralkyl, haloloweralkyl, heterocycloaminoalkyl, and loweralkylaminoloweralkyl.

18. (Original) A compound of claim 17, wherein at least one of R₁, R₂, R₃ and R₄ is loweralkylaminoloweralkyl.

19. (Original) A compound of claim 17, wherein R₁, R₂, and R₃ are hydrogen and R₄ is selected from the group consisting of hydrogen, methyl, ethyl, aminoethyl, dimethylaminoethyl, pyridylethyl, piperidinyl, pyrrolidinylethyl, piperazinylethyl and morpholinylethyl.

20. (Original) A compound of claim 1, wherein at least one of R₅ and R₇ is selected from the group consisting of substituted and unsubstituted aryl, heteroaryl and biaryl.

21. (Currently Amended) A compound of claim 20, wherein at least one of R₅ and R₇ is a substituted or unsubstituted moiety of the formula:



(III)

07 wherein R₁₀, R₁₁, R₁₂, R₁₃, and R₁₄ are independently selected from the group consisting of hydrogen, nitro, amino, cyano, halo, thioamido, carboxyl, hydroxy, and optionally substituted loweralkyl, loweralkoxy, loweralkoxyalkyl, haloloweralkyl, haloloweralkoxy, aminoalkyl, alkylamino, alkylthio, alkylcarbonylamino, aralkylcarbonylamino, heteroaralkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, aminocarbonyl, loweralkylaminocarbonyl, aminoaralkyl, loweralkylaminoalkyl, aryl, heteroaryl, cycloheteroalkyl, aralkyl, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, arylcarbonyloxyalkyl, alkylcarbonyloxyalkyl, heteroarylcarbonyloxyalkyl, aralkylcarbonyloxyalkyl, and heteroaralkylcarbonyloxyalkyl.

22. (Currently Amended) A compound of claim 21, wherein R₁₀, R₁₁, R₁₃, and R₁₄ are hydrogen and R₁₂ is selected from the group consisting of halo, loweralkyl, hydroxy, loweralkoxy, haloloweralkyl, aminocarbonyl, alkylaminocarbonyl and cyano.

23. (Currently Amended) A compound of claim 21, wherein R₁₁, R₁₃, and R₁₄ are hydrogen and R₁₀ and R₁₂ are independently selected from the group consisting of halo, loweralkyl, hydroxy, loweralkoxy, haloloweralkyl and cyano.

24. (Currently Amended) A compound of claim 21, wherein R₁₀, R₁₁, R₁₃, and R₁₄ are hydrogen and R₁₂ is heteroaryl.

25. (Currently Amended) A compound of claim 21, wherein R₁₀, R₁₁, R₁₃, and R₁₄ are hydrogen and R₁₂ is heterocycloalkyl.

26. (Currently Amended) A compound of claim 21, wherein at least one of R₁₀, R₁₁, R₁₂, R₁₃, and R₁₄ are halo and the remainder of R₁₀, R₁₁, R₁₂, R₁₃, and R₁₄ are hydrogen.

27. (Currently Amended) A compound of claim 21, wherein at least one of R₅ and R₇ is selected from the group consisting of dichlorophenyl, difluorophenyl, trifluoromethylphenyl, chlorofluorophenyl, bromochlorophenyl, ethylphenyl, methylchlorophenyl, imidazolylphenyl, cyanophenyl, morphlinophenyl and cyanochlorophenyl.

28. (Original) A compound of claim 1, wherein R₆ is substituted alkyl selected from the group consisting of aralkyl, hydroxyalkyl, aminoalkyl, aminoaralkyl, carbonylaminoalkyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, aralkylcarbonylaminoalkyl, aminoalkoxyalkyl and arylaminoalkyl.

29. (Original) A compound of claim 1, wherein R₆ is substituted amino selected from the group consisting of alkylamino, alkylcarbonylamino, alkoxy carbonylamino, arylalkylamino, arylcarbonylamino, alkylthiocarbonylamino, arylsulfonylamino, heteroaryl amino alkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, aralkylcarbonylamino, and heteroaralkylcarbonylamino.

30. (Original) A compound of claim 1, wherein R₆ is selected from the group consisting of unsubstituted or substituted aminocarbonyl, alkyloxycarbonyl, aryloxycarbonyl, aralkyloxycarbonyl and alkylaminoalkyloxycarbonyl.

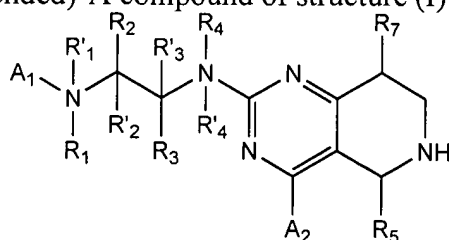
31. (Original) A compound of claim 1, wherein R₆ is selected from the group consisting of amidino, guanidino, cycloimido, heterocycloimido, cycloamido, heterocycloamido, cyclothioamido and heterocycloloweralkyl.

32. (Original) A compound of claim 1, wherein R₆ is aryl.

33. (Original) A compound of claim 1, wherein R₆ is heteroaryl.

34. (Original) A compound of claim 33, wherein R₆ is selected from the group consisting of substituted or unsubstituted pyridyl, pyrimidinyl, thiazolyl, indolyl, imidazolyl, oxadiazolyl, tetrazolyl, pyrazinyl, triazolyl, thienyl, furanyl, quinoliny, pyrrolylpyridyl, benzothiazolyl, benzopyridyl, benzotriazolyl, and benzimidazolyl.

35. (Currently Amended) A compound of structure (I):



08 wherein:

A₁ is optionally substituted aryl or heteroaryl;

A₁ and A₂ are optionally substituted aryl, aryloxy, acylamino or heteroaryl;

R₁, R₂, R₃ and R₄ are independently selected from the group consisting of hydrogen, hydroxyl, and optionally substituted loweralkyl, cycloloweralkyl, alkylaminoalkyl, loweralkoxy, amino, alkylamino, alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, heteroarylcarbonyl, heteroaralkylcarbonyl, aryl and heteroaryl;

R'₁, R'₂, R'₃ and R'₄ are independently selected from the group consisting of hydrogen, and optionally substituted loweralkyl;

R₅ and R₇ are independently selected from the group consisting of hydrogen, hydroxy, halo, carboxyl, nitro, amino, amido, amidino, imido, cyano, and substituted or unsubstituted loweralkyl, loweralkoxy, alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, heteroarylcarbonyl, heteroaralkylcarbonyl, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkylaminocarbonyloxy, arylaminocarbonyloxy, formyl, loweralkylcarbonyl, loweralkoxycarbonyl, aminocarbonyl, aminoaryl, alkylsulfonyl, sulfonamido, aminoalkoxy, alkylamino, arylamino, aralkylamino, heteroarylamino,

heteroaralkylamino, alkylcarbonylamino, alkylaminocarbonylamino, arylaminocarbonylamino, aralkylcarbonylamino, heteroaralkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, amidino, cycloalkyl, cycloamido, cyclothioamido, cycloamidino, heterocycloamidino, cycloimido, heterocycloimido, guanidiny, aryl, biaryl, heteroaryl, heterobiaryl, heterocyclo, heterocycloalkyl, arylsulfonyl and arylsulfonamido;

and the pharmaceutically acceptable salts thereof.

36.-39. (Canceled)

40. (Original) A compound of claim 35, wherein at least one of A₁ and A₂ is an aromatic ring having from 3 to 10 carbon ring atoms and optionally 1 or more ring heteroatoms.

41. (Currently Amended) A compound of claim 35, wherein ~~at least one of A₁ and A₂~~ is optionally substituted carbocyclic aryl, arylamino or aryloxy.

42. (Original) A compound of claim 40, wherein at least one of A₁ and A₂ is optionally substituted heteroaryl.

43. (Currently Amended) A compound of claim 35, wherein ~~at least one of A₁ and A₂~~ is selected from the group consisting of substituted or unsubstituted phenylamino and phenyloxy.

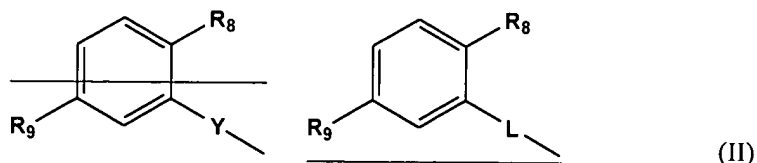
44. (Original) A compound of claim 40, wherein at least one of A₁ and A₂ is selected from the group consisting of substituted or unsubstituted pyridyl, pyrimidinyl, thiazolyl, indolyl, imidazolyl, oxadiazolyl, tetrazolyl, pyrazinyl, triazolyl, thiophenyl, furanyl, quinoliny, purinyl, naphthyl, benzothiazolyl, benzopyridyl, and benzimidazolyl.

45. (Original) A compound of claim 40, wherein at least one of A₁ and A₂ is substituted with at least one and not more than 3 substitution groups.

46. (Original) A compound of claim 45, wherein said substitution groups are independently selected from the group consisting of nitro, amino, cyano, halo, thioamido,

amidino, oxamidino, alkoxyamidino, imidino, guanidino, sulfonamido, carboxyl, formyl, loweralkyl, haloloweralkyl, loweralkoxy, haloloweralkoxy, loweralkoxyalkyl, loweralkylaminoloweralkylcarbonyl, alkylthio, aminoalkyl and cyanoalky.

47. (Currently Amended) A compound of claim 35, wherein at least one of A₁ and A₂ has the formula:



wherein Y or L is -NH- or -O-; and

R₈ and R₉ are independently selected from the group consisting of hydrogen, nitro, amino, cyano, halo, thioamido, amidino, oxamidino, alkoxyamidino, imidino, guanidiny, sulfonamido, carboxyl, formyl, loweralkyl, haloloweralkyl, loweralkoxy, haloloweralkoxy, loweralkoxyalkyl, loweralkylaminoloweralkoxy, loweralkylcarbonyl, loweralkylcarbonyl, lowerheteroalkylcarbonyl, alkylthio, aryl and aralkyl.

48. (Previously Amended) A compound of claim 47, wherein R₈ and R₉ are selected from the group consisting of halo and haloloweralkyl.

49. (Previously Amended) A compound of claim 48, wherein R₈ and R₉ are halo.

012 50. (Currently Amended) A compound of claim 47, wherein ~~at least one of A₁ and~~ A₂ is selected from the group consisting of 2,5-dichlorophenylamino and 2,5-dichlorophenyl.

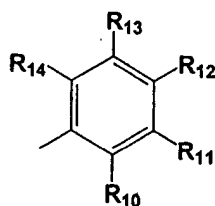
51. (Original) A compound of claim 35, wherein at least one of R₁, R₂, R₃ and R₄ is substituted loweralkyl selected from the group consisting of hydrogen, unsubstituted or substituted loweralkyl, haloloweralkyl, heterocycloaminoalkyl, and loweralkylaminoloweralkyl.

52. (Original) A compound of claim 51, wherein at least one of R₁, R₂, R₃ and R₄ is loweralkylaminoloweralkyl.

53. (Original) A compound of claim 51, wherein R₁, R₂, and R₃ are hydrogen and R₄ is selected from the group consisting of hydrogen, methyl, ethyl, aminoethyl, dimethylaminoethyl, pyridylethyl, piperidinyl, pyrrolidinylethyl, piperazinylethyl and morpholinylethyl.

54. (Original) A compound of claim 35, wherein at least one of R₅ and R₇ is selected from the group consisting of substituted and unsubstituted aryl, heteroaryl and biaryl.

55. (Currently Amended) A compound of claim 54, wherein at least one of R₅ and R₇ is a substituted or unsubstituted moiety of the formula:



(III)

wherein R₁₀, R₁₁, R₁₂, R₁₃, and R₁₄ are independently selected from the group consisting of hydrogen, nitro, amino, cyano, halo, thioamido, carboxyl, hydroxy, and optionally substituted loweralkyl, loweralkoxy, loweralkoxyalkyl, haloloweralkyl, haloloweralkoxy, aminoalkyl, alkylamino, alkylthio, alkylcarbonylamino, aralkyl-carbonylamino, heteroaralkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino aminocarbonyl, loweralkylaminocarbonyl, aminoaralkyl, - loweralkylaminoalkyl, aryl, heteroaryl, cycloheteroalkyl, aralkyl, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, arylcarbonyloxyalkyl, alkylcarbonyloxyalkyl, heteroarylcarbonyloxyalkyl, aralkylcarbonyloxyalkyl, and heteroaralkyl carbonyloxyalkyl.

56. (Currently Amended) A compound of claim 55, wherein R_{10} , R_{11} , R_{13} , and R_{14} are hydrogen and R_{12} is selected from the group consisting of halo, loweralkyl, hydroxy, loweralkoxy, haloloweralkyl, aminocarbonyl, alkylaminocarbonyl and cyano.

57. (Currently Amended) A compound of claim 55, wherein R_{11} , R_{13} , and R_{14} are hydrogen and R_{10} and R_{12} are independently selected from the group consisting of halo, loweralkyl, hydroxy, loweralkoxy, haloloweralkyl and cyano.

013 58. (Currently Amended) A compound of claim 55, wherein R_{10} , R_{11} , R_{13} , and R_{14} are hydrogen and R_{12} is heteroaryl.

59. (Currently Amended) A compound of claim 55, wherein R_{10} , R_{11} , R_{13} , and R_{14} are hydrogen and R_{12} is a heterocycloalkyl.

60. (Currently Amended) A compound of claim 55, wherein at least one of R_{10} , R_{11} , R_{12} , R_{13} , and R_{14} are halo and the remainder of R_{10} , R_{11} , R_{12} , R_{13} , and R_{14} are hydrogen.

61. (Currently Amended) A compound of claim 55, wherein at least one of R_5 and R_7 is selected from the group consisting of dichlorophenyl, difluorophenyl, trifluoromethylphenyl, chlorofluorophenyl, bromochlorophenyl, ethylphenyl, methylchlorophenyl, imidazolylphenyl, cyanophenyl, morphlinophenyl and cyanochlorophenyl.

62. (Original) A compound of claim 35, wherein R_6 is substituted alkyl selected from the group consisting of aralkyl, hydroxyalkyl, aminoalkyl, aminoaralkyl, carbonylaminoalkyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, aralkylcarbonylaminoalkyl, aminoalkoxyalkyl and arylaminoalkyl.

63. (Original) A compound of claim 35, wherein R_6 is substituted amino selected from the group consisting of alkylamino, alkylcarbonylamino, alkoxycarbonylamino, arylalkylamino, arylcarbonylamino, alkylthiocarbonylamino, arylsulfonylamino,

heteroarylamino alkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, aralkylcarbonylamino, and heteroaralkylcarbonylamino.

64. (Original) A compound of claim 35, wherein R_6 is selected from the group consisting of unsubstituted or substituted aminocarbonyl, alkyloxycarbonyl, aryloxycarbonyl, aralkyloxycarbonyl and alkylaminoalkyloxycarbonyl.

65. (Original) A compound of claim 35, wherein R_6 is selected from the group consisting of amidino, guanidino, cycloimido, heterocycloimido, cycloamido, heterocycloamido, cyclothioamido and heterocycloloweralkyl.

66. (Original) A compound of claim 35, wherein R_6 is aryl.

67. (Original) A compound of claim 35, wherein R_6 is heteroaryl.

68. (Original) A compound of claim 67, wherein R_6 is selected from the group consisting of substituted or unsubstituted pyridyl, pyrimidinyl, thiazolyl, indolyl, imidazolyl, oxadiazolyl, tetrazolyl, pyrazinyl, triazolyl, thienyl, furanyl, quinolynyl, pyrrolylpyridyl, benzothiazolyl, benzopyridyl, benzotriazolyl, and benzimidazolyl.

69. (Previously Amended) A pharmaceutical composition comprising an amount of a compound of claim 1 effective to inhibit GSK3 activity in a human or animal subject when administered thereto, together with a pharmaceutically acceptable carrier.

70. (Original) A method of inhibiting GSK3 activity in a human or animal subject, comprising administering to the human or animal subject a composition of claim 69.

71. (Original) A method of treating a cell comprising administering to the cell an amount of a compound of claim 1 effective to inhibit GSK3 activity in the cell.

72. (Previously Amended) A method for treating a disorder associated with excessive GSK3 activity in a human or animal subject, comprising administering to the human or

animal subject an amount of a composition of claim 69 effective to inhibit GSK3 activity in the subject.

73. (Original) A method of claim 72, wherein the composition is administered by a mode of administration selected from the group consisting of oral, subcutaneous, transdermal, transmucosal, iontophoretic, intravenous, intrathecal, buccal, sublingual, intranasal, and rectal administration.

014 74. (Currently Amended) A method of claim 72, wherein said GSK3-mediated disorder is selected from the group consisting of diabetes, obesity, atherosclerotic cardiovascular disease, essential hypertension, polycystic ovary syndrome, ~~syndrome X~~, ischemia, traumatic brain injury, bipolar disorder or cancer.

75.-78. (Canceled)